REMARKS

Claims 2 and 5 have been withdrawn as non-elected claims, without prejudice for prosecution in a continuing or divisional application. The withdrawal of claims are not in acquiescence to any rejection of record.

Claims 1, 3, 4, 6, 7, and 10-18 were examined.

Claims 8 and 9 were not examined previously due to an error in dependency which suggested they were part of the non-elected claims. Claim 8 has been revised to correct a typographic error in its dependency. It is now correctly dependent from claim 7. Claim 9 depends from claim 8. Therefore, claims 8 and 9 should be grouped with the examined claims.

Claims 1, 3, 4, 6-18 have been amended to encompass immunogenic compositions. Support for the amendments to claim 1 is found, in the Specification, at least at: page 7, lines 4-10; page 9, lines 11-16; page 11, lines 15-27; page 13, lines 21-26; page 18, lines 21-24; and in Examples I-IV beginning on page 26, line 1 and ending on page 29, line 14. The amendments are made for business considerations and to better tailor the claims to encompass commercially contemplated embodiments of the invention at the present time. The amendments have not narrowed the scope of the original claims.

No new matter has been introduced, and entry of the amendments is respectfully requested.

Applicants also, have amended the Specification to correct typographical errors.

Claim Rejections under 35 USC §112, second paragraph

Claims 1, 3, 4, 6, 7, 10-12 and 16-18 were rejected under 35 USC §112, second paragraph, as allegedly being indefinite for reciting "complexed with said antigen, a composition comprising proteosomes, bioadhesive nanoemulsions, or both." The Examiner argued that it is unclear what is meant by this phrase. In particular, Examiner argued that it is allegedly "unclear how the antigen is complexed with a composition comprising the proteosomes or nanoemulsions."

Applicants respectfully traverse, as page 8, lines 18-22 in the Specification indicate "the vaccine composition is preferably formed by: (a) bonding the hydrophobic material to the protein

or peptide to form a hydrophobic-hydrophilic compound; and (b) admixing the compound with the proteosomes, bioadhesive nanoemulsions, or both such that the antigen is complexed with the proteosomes or nanoemulsion.

Without acquiescence to the allegation of indefiniteness for the claims as originally presented and in the interest of expediency claim 1, has been rewritten above to clarify the composition complex relationship, which now renders the 35 USC §112, second paragraph rejection for the claims listed as moot.

Claim Rejections under 35 USC §112, first paragraph

Claims 1, 3, 4, 6, 7, and 10-18 were rejected under 35 USC §112, first paragraph, as allegedly failing to "reasonably provide enablement the full scope of the claims" because "Applicant has not demonstrated that any antigen would be an effective vaccine." The Examiner however did state that claim language utilizing an "immunogenic composition" would be sufficient for enablement purposes. Without acquiescence to the allegations of non-enablement for the claims as originally presented, Claims 1, 3, 4, and 6-18 have been revised to encompass immunogenic compositions capable of inducing neutralizing antibodies. We assert that the revised composition claims have not been narrowed in scope.

The claims as rewritten now render 35 USC §112, first paragraph rejection for the claims listed as moot.

Claim Rejections under 35 USC §102(b)

Claims 1, 3, 4, 6, and 10-17 were rejected under 35 USC §102(b) as allegedly anticipated by Lowell *et al.*, *Science* 240(4853):800-02 (1988). Applicants have carefully reviewed the statement of the instant rejection and assert that the rejection is based on the belief that Lowell teaches the claimed compositions particularly as they relate to a "combination of a lauroyl containing hydrophobic material with an antigenic peptide comprising an endogenous hydrophobic sequence, and a proteosome."

Applicants respectfully traverse the instant rejection because Lowell et al. fail to disclose or suggest an exogenous hydrophobic material in a composition with said endogenous

hydrophobic sequence as claimed. Lowell *et al.* also fail to disclose or suggest the use of *neutralizing* antibodies or non-serum mucosal antibodies. Furthermore, Lowell *et al.* fail to disclose or suggest the use of bioadhesive nanoemulsions. In the absence of such a disclosure or suggestion, Lowell *et al.* cannot anticipate the claims. Applicants respectfully request withdrawal of the 35 USC §102(b) rejection in view of these remarks.

Claim Rejections under 35 USC §102(e)

Claims 1, 3, 4, 6, and 10-17 were rejected under 35 USC §102(e) as allegedly anticipated by Lowell *et al.*, U.S. Patent 5,726,292 (the '292 patent). Applicants have carefully reviewed the statement of the instant rejection and respectfully traverse.

Applicants respectfully traverse the instant rejection because the present claims utilize *neutralizing* mucosal antibodies which are not taught or disclosed in the '292 patent reference. Although the '292 patent reference describes antibodies that recognize an antigen, they are not neutralizing antibodies. For example, if the antibody binds to an epitope that is located in a non-critical site of the antigen or a site on the antigen which, when present in the pathogen, is not accessible to the antibody, the antibody will not be neutralizing. Neutralizing antibodies are those that interfere with, or impede, a deleterious or undesired function of the microorganism. Therefore, a neutralizing antibody performs differently than other antibodies. For these reasons, Applicants assert that the '292 patent reference does not anticipate the stated claims and this rejection should be withdrawn.

The Examiner argues that the '292 patent allegedly indicates that proteosome associated antigens are capable of inducing mucosal and respiratory responses, and that mice vaccinated with such constructs were given protection - thereby indicating that the constructs would be effective in inducing neutralizing antibodies.

Applicants also respectfully traverse, since the antibodies actually produced in the '292 patent reference (Columns 18-20) are directed toward serum antibodies rather than mucosal antibodies as claimed, or the antibodies were produced without the use of an exogenous hydrophobic sequence as claimed. Moreover, in those instances in which the '292 patent conjugates conferred protection against subsequent challenge, the protection was against

systemic challenge resulting in high levels of serum antibodies rather than mucosal antibodies. For these reasons, Applicants assert that the '292 patent reference does not anticipate the stated claims and this rejection should be withdrawn.

Applicants respectfully traverse the instant rejection, because the '292 patent reference fail to disclose or suggest the use of bioadhesive nanoemulsions. In the absence of such a disclosure or suggestion, the '292 patent reference cannot anticipate the claims, and this rejection should be withdrawn.

Applicants respectfully request withdrawal of the 35 USC §102(e) rejection in view of these remarks.

Claim Rejections under 35 USC §103(a)

Claims 7 and 18 were rejected under 35 USC §103(a) as allegedly being obvious over Lowell *et al.*, U.S. Patent 5,726,292 (the '292 patent). Applicants have carefully reviewed the statement of the instant rejection and respectfully submit that no *prima facie* case of obviousness has been presented.

Claims 7 and 18 are claims that depend on the claims discussed above regarding the 35 USC §102(e) rejection over the '292 patent. As Examiner is fully aware, each dependent claim contains all of the limitations of the claim from which it depends. The arguments above are therefore incorporated herein to overcome the current rejection. The fact that the '292 patent does not teach mucosal, or neutralizing antibodies, the hydrophobic sequence as claimed is different, and further that the '292 reference does not teach the use of bioadhesive nanoemulsions, all establish that the '292 patent does not teach or suggest the claim elements of the current application.

Accordingly, no *prima facie* case of obviousness is present because the '292 patent reference does not suggest the claimed invention.

Applicants respectfully request withdrawal of the 35 USC §103(a) rejection in view of these remarks.

Claims 7 and 18 were rejected under 35 USC §103(a) as allegedly being obvious over the '292 patent as applied to claims 1, 3, 4, 6, and 10-17 above, and further in view of VanCott *et al.*, *J immunol Methods* 183:103-17 (1995). Applicants have carefully reviewed the statement of the instant rejection and respectfully traverse.

The VanCott reference does not remedy the deficiencies of the Lowell reference, which is discussed above. Although VanCott (described in the Specification, beginning on page 5 line 20 through page 6 line 12) provides an assessment of the oligomeric structure and antigenic properties of purified gp160 protein, it describes serum antibodies only. Therefore, it does not discuss how to generate the claimed neutralized mucosal antibodies, nor does the VanCott reference utilize a proteosome complex or nanoemulsion. Moreover, VanCott does not disclose the significance of hydrophobic peptide portions of oligomeric gp160 nor its complexing with proteosomes.

Accordingly, no *prima facie* case of obviousness is present because the '292 patent reference in combination with the VanCott reference does not disclose or suggest all the elements of the claims.

Applicants respectfully request withdrawal of the 35 USC §103(a) rejection in view of these remarks.

Claims 1, 3, 4, 6, 7, 10, 11, 16-18 were rejected under 35 USC §103(a) as allegedly unpatentable over any of the '292 patent, Lowell, or Lowell in view of VanCott as applied above, and further in view of WO 95/11700 (the PCT reference). Applicants have carefully reviewed the statement of the instant rejection and respectfully traverse.

As previously argued individually for the Lowell, '292 patent and VanCott references, all the claim elements were not met with any of these references alone or when combined. The PCT reference alone or in combination with the other references also does not remedy the deficiencies of these references for the following additional reasons.

The PCT reference is specifically concerned with oil-in-water submicron emulsions (SMEs) as a vaccine adjuvant and does not teach or suggest successful use of an exogenous proteosome in the antigen complex to elicit neutralizing secretion antibodies as claimed. Based

on the PCT reference, it would not be obvious to a skilled person to try and modify a protein antigen with a hydrophobic addition or to select an oligomeric gp160 protein antigen, and complex the modified or gp160 antigen to proteosomes in the hope of producing a immunogenic composition capable of inducing neutralizing secretion antibodies.

Applicants also maintain that the PCT reference does not suggest or teach the use of oligomeric gp160. The PCT reference does not demonstrate the production of neutralizing secretion antibodies against the oligomeric gp160 protein or suggest that this could be achieved using a composition such as that in claim 8 (please note that claim 8 was not examined previously due to an error in dependency as explained before. Claim 8 has been revised to correct a typographic error in its dependency and therefore should be grouped with the examined claims). In fact the PCT reference does not demonstrate production of neutralizing secretion antibodies at all. By contrast, Example 9 of the present application successfully demonstrates the induction of neutralizing secretion antibodies using the present oligomeric gp160 compositions.

Applicants respectfully request withdrawal of the 35 USC §103(a) rejection in view of these remarks.

Double Patenting Claim Rejections

Claims 1, 3, 4, 6, 7, 10-18 were rejected as allegedly being unpatentable over claims 1, 2, 5, 7, and 8 of the '292 patent for non statutory obviousness-type double patenting. The Examiner claims that the functional language of the present claims merely illustrates an inherent property of the invention claimed by the 292 patent. Applicants have carefully reviewed the statement of the instant rejection and respectfully traverse.

As stated above, the constructs claimed in the '292 patent differ from those in the current application, these differences have been described above for both the 35 USC §102(e) and §103(a) rejections over the same art.

The claims and processes of the two documents differ in that there are various hydrophobic sequences, complexed with proteosomes and/or bioadhesive nanoemulsions, which are used to create different constructs that enables the present application to produce non-serum neutralizing antibodies rather than the serum non-neutralizing antibodies of the '292 patent.

Accordingly, no *prima facie* case of obviousness-type double-patenting is present because the '292 patent reference is patentably distinct in that it does not disclose or suggest all the elements of the claims.

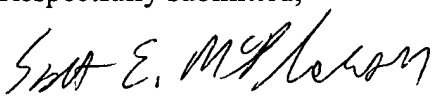
Applicants respectfully request withdrawal of the Double Patenting Claim rejection in view of these remarks.

Conclusion

In light of the above amendments and arguments, Applicants respectfully submit that claims 1, 3, 4, and 6-18 are in condition for allowance and respectfully urge early indication to this effect.

If the Examiner believes a telephone conference would expedite prosecution of this application, he is encouraged to telephone the undersigned at the number provided below.

Respectfully submitted,



Scott E. McPherson
Reg. No. 53,307

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (858) 350-6143
Fax: (650) 326-2422